PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Manoharan et al.

Serial No.: 09/970,971

Filing Date: October 4, 2001

Group Art Unit: Not yet assigned

Examiner: Not yet assigned

OLIGONUCLEOTIDES HAVING A-DNA FORM AND B-DNA FORM

CONFORMATIONAL GEOMETRY

DATE OF DEPOSIT: December 17, 2001

I HEREBY CERTIFY THAT THIS PAPER IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL, POSTAGE PREPAID ON THE DATE INDICATED ABOVE AND IS ADDRESSED TO THE ASSISTANT COMMISSIONER FOR PATENTS,

SHINGTON, DO

TYPED NAME: Emma R. Dailey REGISTRATION NO.: 48,491

Assistant Commissioner for Patents Washington, D.C. 20231

Dear Sir:

For:

INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 C.F.R. §1.56 and in accordance with 37 C.F.R. §§1.97-1.98, information relating to the above-identified application is hereby disclosed. Inclusion of information in this statement is not to be construed as an admission that this information is material as that term is defined in 37 C.F.R. §1.56(b).

 \boxtimes In accordance with §1.97(b), since this Information Disclosure Statement is being

filed either within three months of the filing date of the above-identified application, within three months of the date of entry into the national stage of the above identified application as set forth in §1.491, before the mailing date of a first Office Action on the merits of the above-identified application, or before the mailing date of a first office action after the filing of request for continued examination under §1.114, no additional fee is required.

	In accordance with §1.129(a), this Information Disclosure Statement is being
	filed in connection with \square the first or \square second After Final Submission,
	therefore:
	☐ Certification in Accordance with §1.97(e) is attached; or
	The fee of $$180.00$ as set forth in $$1.17(p)$ is attached.
	In accordance with §1.97(c), this Information Disclosure Statement is being filed
	after the period set forth in §1.97(b) above but before the mailing date of either a Final Action under §1.113 or a Notice of Allowance under §1.311, or before an action that otherwise closes prosecution in the application, therefore:
	☐ Certification in Accordance with §1.97(e) is attached; or
	The fee of $$180.00$ as set forth in $$1.17(p)$ is attached.
	In accordance with §1.97(d), this Information Disclosure Statement is being filed
	after the mailing date of either a Final Action under §1.113 or a Notice of Allowance under §1.311 but before, or simultaneously with, the payment of the Issue Fee, therefore included are: Certification in Accordance with §1.97(e); and the submission fee of §180.00 as set forth in §1.17(p).
	Copies of each of the references listed on the attached Form PTO-1449 are enclosed herewith.
\boxtimes	Copies of references listed on the attached Form PTO-1449 are enclosed herewith
	EXCEPT THAT:
	In view of the voluminous nature of references ES-EV, and the likelihood
	that these references were available to the Examiner, copies were not enclosed with the Information Disclosure Statement filed in Serial No. 09/303,586.

- In accordance with §1.98(d), copies of the following references listed on the attached Form PTO-1449 are not enclosed herewith because they were previously cited by or submitted to the U.S. Patent and Trademark Office in patent application(s) for which a claim for priority under 35 U.S.C.§120 have been made in the instant application:
- Copies of references AA-EV, GT-HO, IR-JC and JG listed on the attached Form PTO-1449 were previously cited by or submitted to the Patent and Trademark Office in prior application Serial No. 09/303,586, filed May 3, 1999. Copies of references EW-GS, HP-IQ and JI were previously cited by or submitted to the Patent and Trademark Office in prior application Serial No. 08/936,166, filed September 23, 1997, now U.S. Patent No. 6,307,040.
 - If any of the foregoing publications are not available to the Examiner, Applicant will endeavor to supply copies at the Examiner's request.

Copies of newly cited references JD-JF, JH and JJ are enclosed herewith.

Serial No. 08/837,201 filed April 14, 1997; Serial No. 09/044,506 filed March 19, 1998 and Serial No. 09/062,416 filed April 17, 1998, were previously cited in the parent application Serial No. 09/303,586 filed May 3, 1999, and have now issued as U.S. Patent Nos. 5,985,558 (JD), 5,955,443 (JE) and 6,111,094 (JF), respectively.

Prior application Serial No. 08/936,166 filed September 23, 1997 is now U.S. Patent No. **6,307,040 (JJ)**.

Please charge any deficiency or credit any overpayment to Deposit Account No. 23-3050. This form is submitted in duplicate.

English language abstracts were provided for those listed references which are not in the English language.

Date: December 17,2001

Emma R. Dailey

Registration No. 48,491

WOODCOCK WASHBURN LLP One Liberty Place - 46th Floor Philadelphia, PA 19103

Telephone: (215) 568-3100 Facsimile: (215) 568-3439

© 2001 WW

Serial No. **09/970,971**

FEB 26 2002 PLEASE		
Form PTO-1449 Modified	Docket No. ISIS-4789	
List of Patent and Publications Cited by Applicant (Use several sheets if necessary)	Applicant Manoharan et al.	
U.S. Department of Commerce Patent and Trademark Office	Filing Date October 4, 2001	
OTHER DOCUMENTS (Including A	author Title Date Pertiner	1

1			L				
	List of Patent and Publications Cited by Applicant (Use several sheets if necessary)						
	Department of Commerce at and Trademark Office	Filing Date October 4, 2001	Group Not yet assigned				
ОТНЕ	OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)						
AA	Abe, A. et al., "Conformational Energy Dipole Moments of Polyoxides CH30 6468-6476						
AB	Albert, P.R. et al., "Antisense knocke signal transduction", <i>Trends Pharmae</i>	_	_				
AC	AC Altmann, K. et al., "Second Generation Antisense Oligonucleotides-Inhibition of Pkc-1 And c-RAF Kinase Expression by Chimeric Oligonucleotides Incorporating 6-Substituted Carbocyclic Nucleosides and 2'-O-Ethylene Glycol Substituted Ribonucleosides," Nucleosides & Nucleotides, 1997, 16(7-9), 917-926		ides Incorporating 6- col Substituted				
AD	Altmann, K. et al., "Second-Generation Antisense Oligonucleotides: Structure-Activity Relationships and the Design of Improved Signal-Transduction Inhibitors", <i>Biochem. Soc. Trans.</i> , 1996 , <i>24</i> , 630-637						
AE	Altmann, K. et al., "Second Generation of Antisense Oligonucleotides: From Nuclease Resistance to Biological Efficacy in Animals," <i>Chimia</i> , 1996 , <i>50</i> , 168-176						
AF :	Baker, B.F. et al., "2'-O-(2-Methoxy)ethyl-modified Anti-intercellular Adhesion Molecule 1 (ICAM-1) Oligonucleotides Selectively Increase the ICAM-1 Translation Initiation Complex in Human Umbilical Vein Endothelial Cells", <i>J. Biol. Chem.</i> , 1997 , <i>272</i> , 11994-12000						
AG	Beal, P. A. et al., "Second Structural Motif for Recognition of DNA by Oligonucleotide-Directed Triple-Helix Formation," <i>Science</i> , 1991 , <i>251</i> , 1360-1363						
АН	Beaucage, S.L. et al., "Advances in the Synthesis of Oligonucleotides by the Phosphoramidite Approach", <i>Tetrahedron</i> , 1992 , 48, 2223-2311						
AI	AI Berger et al., "Crystal structures of B-DNA with incorporated 2'-deoxy-2'-fluoro-arabino-furanosyl thymines: implications of conformational preorganization for duplex stability," <i>Nucl. Acids Res.</i> , 1998 , <i>26(10)</i> , 2473-2480						
AJ	AJ Berkow et al. (eds.), The Merck Manual of Diagnosis and Therapy, 15th Edition, Rahway, N.J., 1987, 2263-2277						
EXAMINER		DATE CONSIDER	ED				
			· · · · · · · · · · · · · · · · · · ·				

	FEB 2 6 2002 SEE		
Form	PTO-1449 Modified	Docket No. ISIS-4789	Sheet 2 of 21 Serial No. 09/970,971
	f Patent and Publications Cited by Applicant everal sheets if necessary)	Applicant Manoharan et al.	
1	Department of Commerce at and Trademark Office	Filing Date October 4, 2001	Group Not yet assigned
ОТНЕ	CR DOCUMENTS (Including Autho	r, Title, Date, Pertine	nt Pages, Etc.)
AK	Berkow et al. (eds.), <i>The Merck Man</i> Rahway, N.J., 1987 , 2283-2287	ual of Diagnosis and I	Therapy, 15th Edition,
AL	Berkow et al. (eds.), <i>The Merck Man</i> Rahway, N.J., 1987 , 2286-2293	ual of Diagnosis and I	Therapy, 15th Edition,
AM	AM Berkow et al. (eds.), The Merck Manual of Diagnosis and Therapy, 15th Edition, Rahway, NJ, 1987, 2301-2310		
AN	AN Bernhard, E.J. et al., "Direct Evidence Linking Expression of Matrix Metalloproteinase 9 (92-kDa gelatinase/collagenase) to the metastatic phenotype in transformed rat embryo cells," <i>Proc. Natl. Acad. Sci. USA</i> , 1994 , <i>91</i> , 4293-4297		
AO	AO Birkedal-Hansen, H. et al., "Proteolytic Remodeling of Extracellular Matrix," <i>Curr. Op. Cell Biol.</i> , 1995 , 7, 728-735		
AP	AP Bock, L. C. et al., "Selection of Single-Stranded DNA Molecules that Bind and Inhibit Human Thrombin," <i>Nature</i> , 1992, 355, 564-566		
AQ	Böggemeyer, E. et al., "Borrelia Burselectin, P-selectin, ICAM-1 and VC Cell Adhes. Commun., 1994, 2, 145-	AM-1 on Mouse Endo	
AR	AR Conte, M. R. "Confirmational Properties and Thermodynamics of the RNA Duplex r(CGCAAAUUUGCG)2: Comparison with the DNA Analogue d(CGCAAATTTGCG)2," Nucl. Acids Res., 1997, 25(13), 2627-2634		
AS	AS Cornell, W. D. et al., "A Second Generation Force Field for the Simulation of Proteins Nucleic Acids, and Organic Molecules," J. Am. Chem. Soc., 1995, 117, 5179-5197		
AT	AT Cory, A.H. et al., "2'-Deoxy-2'-Methylene Derivatives of Adenosine, Guanosine, Tubercidin, Cytidine and Uridine as Inhibitors of L1210 Cell Growth in Culture," Biochem. Pharmacol., 1994, 47(2), 365-371		
EXAMINER		DATE CONSIDER	ED

	PE 7050 SOLLOW		Shoot 2 of 21
Form	PTO-1449 Modified	Docket No. ISIS-4789	Sheet 3 of 21 Serial No. 09/970,971
	f Patent and Publications Cited by Applicant everal sheets if necessary)	Applicant Manoharan et al.	
1	Department of Commerce nt and Trademark Office	Filing Date October 4, 2001	Group Not yet assigned
ОТНЕ	ER DOCUMENTS (Including Author	, Title, Date, Pertine	nt Pages, Etc.)
AU	Cowsert, L. M. et al., "In vitro and In Potential for Clinical Development,"		
AV	Crooke, S.T. et al., "Pharmacokinetic Analogs in mice", <i>J. Pharmacol. Exp</i>	-	_
AW	Crooke, S.T. et al., "Kinetic character various antisense oligonucleotide-RN		_
AX	Crooke, S. T., "Progress in Antisense 1996, 16(4), 319-344	Therapeutics," <i>Medic</i>	inal Research Reviews,
AY	Damha, M.J. et al., "An improved probeads for solid-phase oligonucleotide		- -
AZ	Damha et al., "Hybrids of RNA and A Substrates of Ribonuclease H," J. Am	•	•
ВА	De Mesmaeker, A. et al., "Antisense 366-374	Oligonucleotides", Acc	c. Chem. Res., 1995 , 28,
ВВ	Dean, N.M. et al., "Inhibition of prote administration of phosphorthioate and Acad. Sci., 1994, 91, 11762-11766		•
ВС	DeLisser, H. M. et al., "Molecular and Functional Aspects of PECAM-1/CD31," <i>Immunol. Today</i> , 1994 , <i>15(10)</i> , 490-494		
BD	Dimock, S. et al., "An Efficient Multigram Synthesis of Monomers for the Preparation of Novel Oligonucleotides Containing Isosteric Non-Phosphorous Backbones," <i>Nucleosides & Nucleotides</i> , 1997 , <i>16</i> (7-9), 1629-1632		
BE	Downward, J. et al., "The ras Superfamily of Small GTP-binding proteins," <i>TIBS</i> , 15, 1990, 469-472		
BF	BF Egli, M. et al., "RNA Hydration: A Detailed Look," Biochemistry, 1996, 35, 8489-8494		
BG	Englisch, U. et al., "Chemically Mod Angew. Chem. Int. Ed. Eng., 1991, 36		as Probes and Inhibitors",
EXAMINER		DATE CONSIDER	ED

Form PTO-1449 Modified Docket No. Serial No.	of 21		
Form PTO-1449 Modified Docket No. Serial No.			
ISIS-4789 09/970,971			
List of Patent and Publications Cited by Applicant (Use several sheets if necessary) Applicant Manoharan et al.			
U.S. Department of Commerce Patent and Trademark Office Filing Date October 4, 2001 Not yet assigned			
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
BH Fedoroff, O. Y. et al., "Structure of a DNA: RNA Hybrid Duplex Why Rnase I Not Cleave Pure RNA," J. Mol. Biol., 1993, 233, 509-523	ł Does		
BI Flanagan et al., "Cellular penetration and antisense activity by a phenoxazine-substituted heptanucleotide," <i>Nat. Biotechnol.</i> , 1999, 17(1), 48-52			
BJ Fraser, A. et al., "Synthesis and Conformational Properties of 2'-Deoxy-2'-met pyrimidine and -purine Nucleosides: Potential Antisense Applications," J. Hete Chem., 1993, 30, 1277-1287	-		
BK Freier, S.M. et al., "The ups and downs of nucleic acid duplex stability: structus stability studies on chemically-modified DNA:RNA duplexes", <i>Nucl. Acids Re</i> 1997, 25, 4429-4443			
BL Gaffney, B.L. et al., "A New Strategy for the Protection of Deoxyguanosine D Oligonucleotide Synthesis", <i>Tetrahedron Letts.</i> , 1982 , <i>23</i> , 2257-2260	ıring		
BM Gao, Y-G. et al., "Molecular Structure of a DNA Decamer Containing an Antic Nucleoside Arabinosylcytosine: Conformational Pereturbation by Arabinosylc in B-DNA," <i>Biochem.</i> , 1991 , <i>30(41)</i> , 9922-9931			
BN Gmeiner, W.H. et al., "Effect of Cytarabine on the NMR Structure of a Model Okazaki Fragment from the SV40 Genome," <i>Biochem.</i> , 1999 , <i>38</i> , 1166-1175			
Gonzalez, C. et al., "Structure and Dynamics of a DNA-RNA Hybrid Duplex version of the Chral Phosphorothioate Moiety: NMR and Molecular Dynamics with Convent and Time-Averaged Restraints," <i>Biochemistry</i> , 1995 , <i>34</i> , 4969-4982			
BP Gotfredsen, C.H. et al., "Novel Oligodeoxynucleotide Analogues Containing A Methylarabinonucleoside," <i>Tetra. Lett.</i> , 1994 , <i>35(37)</i> , 6941-6944	Gotfredsen, C.H. et al., "Novel Oligodeoxynucleotide Analogues Containing A 2'-O-Methylarabinonucleoside," <i>Tetra. Lett.</i> , 1994 , <i>35(37)</i> , 6941-6944		
BQ Gotfredsen, C.H. et al., "Synthesis and Properties of α- and β-Oligodeoxynurle Containing α- and β-1-(2-O-Methy-D-arabino-furanosyl)thymine," Bioorg. Methodson, 1996, 4(8), 1217-1225			
BR Gotfredsen, C.H. et al., "Structure of a DNA Duplex Containing a Single 2'-O-Methyl-β-p-araT: Combined Use of NMR, Restrained Molecular Dynamics, ar Relaxation Matrix Refinement," Bioconjugate Chem., 1996, 7, 680-688	d Full		
EXAMINER DATE CONSIDERED			

. •	PE JOSO DELLA		Sheet 5 of 21
Forn	n PTO-1449 Modified	Docket No. ISIS-4789	Serial No. 09/970,971
	of Patent and Publications Cited by Applicant several sheets if necessary)	Applicant Manoharan et al.	
	Department of Commerce nt and Trademark Office	Filing Date October 4, 2001	Group Not yet assigned
ОТН	ER DOCUMENTS (Including Autho	r, Title, Date, Pertine	nt Pages, Etc.)
BS	Griffin, L. C. et al., "In Vivo Anticoa Thrombin Inhibitor and Demonstratio Circuits," <i>Blood</i> , 1993 , <i>81</i> , 3271-327	on of Regional Anticoa	
ВТ	Griffiths, C.E.M. et al., "Keratinocyte Expression Precedes Derman T Lyn Dermatitis (<i>Rhus dermatitis</i>)", <i>Am. J.</i>	nphocyte Infiltration in	Allergic Contact
BU	Gum, R. et al., "Stimulation of 92-kDa Gelatinase B Promoter Activity by ras Is Mitogen-activated Protein Kinase Kinase 1-independent and Requires Multiple Transcription Factor Binding Sites Including Closely Spaced PEA3/ets and AP-1 Sequences," J. Biol. Chem., 1996, 271(18), 10672-10680		
BV	Guzaev A. et al., "Synthesis of C-Radiolabeled Oligonucleotides with a Novel Phosphoramidite Reagent," <i>Bioorg. & Med. Chem. Lett.</i> , 1998 , <i>8</i> , 1123-1126		
BW	Hakugawa, J. et al., "The Inhibitory I Eosinophil Infilration in Cutaneous I with Ovalbumin (OVA)," J. Dermato	ate Phase Response in	
BX	Hansske, F. et al., "2' and 3'-Ketonuc Products", Tetrahedron, 1984, 40, 12		pino and Xylo Reduction
BY	Hansske et al., "Nucleic Acid Related the Synthesis of 2' and 3'-Ketonucleo	-	
BZ	Hegemann, L. et al., "Biochemical Pharmacology of Protein Kinase C and its Relevance for Dermatology", <i>Pharmacology of the Skin</i> , 1992 , <i>Ch. 22</i> , CRC Press, Boca Raton, 357-368		
CA	Himelstein, B. P. et al., "Metalloproteinases in Tumor Progression: The Contribution of MMP-9," <i>Invasion & Metastasis</i> , 1994-95 , <i>14</i> , 246-258		
СВ	CB Ho, V.C. et al., "Treatment of severe lichen planus with cyclosporine", J. Am. Acad. Dermatol., 1990, 22, 64-68		
СС	CC Horton, N. C. et al., "The Structure of an RNA/DNA Hybrid: A Substrate of the Ribonuclease Activity of HIV-1 Reverse Transcriptase," J. Mol. Biol., 1996, 264, 521-533		
EXAMINER		DATE CONSIDER	ED



Form	PTO-1449 Modified	Docket No. ISIS-4789	Serial No. 09/970,971	
	List of Patent and Publications Cited by Applicant (Use several sheets if necessary)		Applicant Manoharan et al.	
	Department of Commerce t and Trademark Office	Filing Date October 4, 2001	Group Not yet assigned	
ОТНЕ	R DOCUMENTS (Including Author	r, Title, Date, Pertine	nt Pages, Etc.)	
CD	Hua, J. et al., "Inhibition of Matrix Me Metastasis in a Rat Sarcoma Model Syst			
CE	Hurtenbach, U. et al., "Prednisolone Inflammatory Tissue Destruction in Santa Int. J. Immunopharmac, 1996, 18, 28	Scid Mice Infected with		
CF	Iribarren, A.M. et al., "Resistance to Degradation by Nucleases of (2'S)-2'-Deoxy-2'-C-methyloligonucleotides, Novel Potential Antisense Probes," <i>Antisense Res. Dev.</i> , 1994 , 4(2), 95-98			
CG	Iyer, R.P. et al., "The Automated Synthesis of Sulfur-Containing Oligodeoxyribonucleotides Using 3H-1,2-Benzodithiol-3-one 1,1-Dioxide as a Sulfur-Transfer Reagent", <i>J. Org. Chem.</i> , 1990 , <i>55</i> , 4693-4699			
СН	Jaishree, T.N. et al., "Structural Influence of RNA Incorporation in DNA: Quantitative Nuclear Magnetic Resonance Refinement of d(CG)r(CG)d(CG) and d(CG)r(C)d(TAGCG)," <i>Biochem.</i> , 1993 , <i>32</i> , 4903-4911			
CI	Kabanov, A.V.,"A new class of antivirals: antisense olgonucleotides combined with a hydrophobic substituent effectively inhibit influenza virus reproduction and synthesis of virus-specific proteins in MDCK cells", <i>FEBS Letts.</i> , 1990 , <i>259</i> , 327-330			
CJ	Katocs, A.S. et al., "Biological Testir Ed., Gennaro (ed.), Mack Publishing			
СК	Kerr, L. D. et al., "TGF-\(\mathcal{B}\)1 Inhibition of Transin/Stromelysin Gene Expression Is Mediated Through a Fos Binding Sequence," Cell, 1990, 61, 267-278			
. CL	Kerr, L. D. et al., "Growth Factors Regulate Transin Gene Expression by c-fos- Dependent and c-fos-Independent Pathways," <i>Science</i> , 1988 , <i>242</i> , 1424-1427			
СМ	Kois, P. et al., "Synthesis and Some Properties of Modified Oligonucleotides. 2. Oligonucleotides Containing 2'-Deoxy-2'-Fluoro-β-D-Arabinofuranosyl Pyrimidine Nucleosides," <i>Nucleosides Nucleotides</i> , 1993 , <i>12(10)</i> , 1093-1109			
CN	CN Kroschwitz, J.I., "Polynucleotides", Concise Encyclopedia of Polymer Science and Engineering, 1990, John Wiley & Sons, New York, 858-859			
EXAMINER		DATE CONSIDER	ED	

PE VOS
EB 20 Los
PATEME TO MILITER

Form	PTO-1449 Modified	Docket No. ISIS-4789	Serial No. 09/970,971
	f Patent and Publications Cited by Applicant everal sheets if necessary)	Applicant Manoharan et al.	
	Department of Commerce at and Trademark Office	Filing Date October 4, 2001	Group Not yet assigned
ОТНЕ	R DOCUMENTS (Including Author	r, Title, Date, Pertine	nt Pages, Etc.)
СО	Lane, A. N. et al., "NMR Assignments Hybrid Duplex d(GTGAACTT)-r(AAG		
СР	Lesnik, E.A. et al., "Oligodeoxynucle Synthesis and Effects on Stability of 7832-7838	_	
CQ	Lesnik, E. A. et al., "Relative Thermodynamic Stability of DNA, RNA, and DNA: RNA Hybrid Duplexes: Relationship with Base Composition and Structure," <i>Biochemistry</i> , 1995 , <i>34</i> (<i>34</i>), 10807-10815		
CR	Letsinger, R.L. et al., "Cholesteryl-conjugated oligonucleotides: Synthesis, properties and activity as inhibitors of replication of human immunodeficiency virus in cell culture", <i>Proc. Natl. Acad. Sci.</i> , 1989 , <i>86</i> , 6553-6556		
CS	Lima et al., "Binding Affinity and Specificity of <i>Escherichia coli</i> RNase H1: Impact on the Kinetics of Catalysis of Antisense Oligonucleotide - RNA Hybrids," <i>Biochemistry</i> , 1997 , <i>36</i> , 390-398		
CT	Lin et al., "A Cytosine Analogue Capable of Clamp-Like Binding to a Guanine in Helical Nucleic Acids," <i>J. Am. Chem. Soc.</i> , 1998 , <i>120</i> , 8531-8532		
CU	Lisby, S. et al., "Intercellular adhesion inflammation", Br. J. Dermatol., 198	· ·	1) expression correlated to
CV	Litwin, M. et al., "Novel Cytokine-independent Induction of Endothelial Adhesion Molecules Regulated by Platelet/Endothelial Cell Adhesion Molecule (CD31)," <i>J. Cell Biol.</i> , 1997, 139(1), 219-228		
CW	Manoharan, M. et al., "Lipidic Nucleic Acids", Tetrahedron Letts., 1995, 36, 3651-3654		
CX	CX Manoharan M. et al., "Cholic Acid-Oligonucliotide Conjugates for Antisense Applications", <i>Bioorganic Med. Chem. Letts.</i> , 1994 , <i>4</i> , 1053-1060		
CY	Manoharan M. et al.,"Oligonucleotid Properties of Antisense Agents", Nuc	2 0	
EXAMINER		DATE CONSIDER	ED



Fo	rm	PTO-1449 Modified	Docket No. ISIS-4789	Serial No. 09/970,971
			Applicant Manoharan et al.	
	U.S. Department of Commerce Patent and Trademark Office			Group Not yet assigned
O	THE:	R DOCUMENTS (Including Author	r, Title, Date, Pertine	nt Pages, Etc.)
С	Z	Manoharan, M. et al., "Chemical Mod Bioavailability of Antisense Oligonuc 660, 306-309	-	-
D	A	Manoharan, M. et al., "Introduction of Groove of Nucleic Acids for Antisent 1993, 3, 2765-2770		
D	В	Martin, P., "Ein neuer Zugang zu 2'-Oligonucleotide", Helvetica Chemica	•	_
D	C	Matsuda, A. et al., "Nucleosides and Nucleotides. 97. Synthesis of New Broad Spectrum Antineoplastic Nucleosides, 2'-Deoxy-2'-methylidenecytidine (DMDC) and Its Derivatives," <i>J. Med. Chem.</i> , 1991, 34, 812-819		
D	D	Miller, P.S. et al., "A New approach to chemotherapy based on molecular biology and nucleic acid chemistry: Matagen (masking tape for gene expression)", <i>Anti-Cancer Drug Des.</i> , 1987, 2, 117-128		
D	E	Milligan, J. F. et al., "Current Concepts in Antisense Drug Design," J. Med. Chem., 1993, 36(14), 1923-1937		
D	F	Mishra, R.K. et al., "Improved leishmanicidal effect of phosphorotioate antisense oligonucleotides by LDL-medicated delivery", <i>Biochim. et Biophysica</i> , 1995 , <i>1264</i> , 229-237		
D	G	Monia, B.P. et al., "Sequence-specific Antitumor Activity of a Phosphorothioate Oligodeoxyribonucleotide Targeted to Human C-raf Kinase Supports an Antisense Mechanism of Action In Vivo," <i>Proc. Natl. Acad. Sci. USA</i> , 1996 , <i>93</i> , 15481-15483		
D	Н	Newman, P. J. et al., "Perspective Series: Cell Adhesion in Vascular Biology," Biology PECAM-1, J. Clin. Invest., 1997, 99(1), 3-7		
D	I	Nies, A.S. et al., "Principles of Therapeutics", Goodman & Gilman's The Pharmacological Basis of Therapeutics, 9th Ed., Hardman et al. (eds.), McGraw-Hill, New York, NY, 1996, Ch. 3, 43-62		
EXAMINER			DATE CONSIDER	ED

	FEB 2 6 2002 355		
Earne	PTO-1449 Modified	Docket No.	Sheet 9 of 21 Serial No.
Form	P1O-1449 Wiodined	ISIS-4789	09/970,971
	f Patent and Publications Cited by Applicant everal sheets if necessary)	Applicant Manoharan et al.	
	Department of Commerce at and Trademark Office	Filing Date October 4, 2001	Group Not yet assigned
ОТНЕ	CR DOCUMENTS (Including Author	r, Title, Date, Pertine	nt Pages, Etc.)
DJ	Oberhauser, B. et al., "Effective incoming liposomes and enhanced cell associate Nucl. Acids Res., 1992, 20, 533-538	-	_
DK	Obika et al., "Preparation and Proper Containing 3'-O, 4'-C-Methyleneribo 515-518		- ·
DL	Pon, R.T., "Solid Phase Supports for Oligonucleotide Synthesis", <i>Methods in Molecular Biology, Vol. 20, Protocols for Oligonucleotides and Analogs</i> ", Agrawal, S. (ed.), Humana Press, Totowa, NJ, 1993 , <i>Chapter 19</i> , 465-496		
DM	Regezi, J. A. et al., "Vascular Adhesion Molecules in Oral Lichen Planus," Oral Surg. Oral Med. Oral Pathol., 1996, 81, 682-690		
DN	Resmini, M. et al., "Synthesis of an A Chem. Lett., 1994, 4(16), 1909-1912	Arabinonucleic Acid (ta	ANA)," Bioorg. Med.
DO	Resmini, M. et al., "38. Nucleosides: Arabinoguanosine Building Blocks,"		
DP	Resmini et al., "9. Nucleotides: Part 2 Phosphoramidite Building Blocks," F	•	
DQ	Roberts, D. D. et al., "Neighboring Methoxy Group Effect in Solvolysis Reactions of Cyclopentyl and Cyclohexyl p-Toluenesulfonates," <i>J. Org. Chem.</i> , 1997 , <i>62</i> , 1857-1859		
DR	Roberts, D. D. et al., "Neighboring-Group Study in Solvolyses of Cyclopentyl and Cyclohexyl Tosylates," <i>Cyclopentyl and Cyclohexyl Toslates</i> , 1969 , <i>34(8)</i> , 2415-2417		
DS	Robins, M.J. et al., "Nucleic Acid Re the Efficient Deoxygenation of Secon Stereoselective Conversion of Ribons Chem. Soc., 1983, 105, 4059-4065	ndary Alcohols. Regio	specific and
DT	Rosenthal et al., "Nucleosides of Brand Aminomethyol Sugars," Tetra. Lett.,		hyl, Cyanomethyl, and
EXAMINER		DATE CONSIDER	ED

CATERIAL AND		Sheet 10 of 21		
Form	Form PTO-1449 Modified		Serial No. 09/970,971	
	f Patent and Publications Cited by Applicant everal sheets if necessary)	Applicant Manoharan et al.		
	Department of Commerce at and Trademark Office	Filing Date October 4, 2001	Group Not yet assigned	
ОТНЕ	ER DOCUMENTS (Including Autho	r, Title, Date, Pertine	nt Pages, Etc.)	
DU	Ruoslahti, E., "How Cancer Spreads,	" Sci. Am., 1996, 72-7"	7	
DV	Saison-Behmoaras, T. et al., "Short nagainst Ha-ras point mutation induce cells proliferation", EMBO J., 1991,	selective cleavage of		
DW	Sanghvi, Y.S. et al., "Concept, Discovery and Development of MMI Linkage: Sto of a Novel Linkage for Antisense Constructs," <i>Nucleosides & Nucleotides</i> , 1997 , 16(7-9), 907-916			
DX	Schmit, C. et al., "The Effects of 2'- and 3'-Alkyl Substituents on Oligonucleotide Hybridization and Stability," <i>Bioorg. Med. Chem. Lett.</i> , 1994 , <i>4(16)</i> , 1969-1974 Schweitzer, B.I. et al., "Solution Structure of a DNA Dodecamere Containing the Anti-Neoplastic Agent Arabinosylcytosine: Combined Use of NMR, Restrained Molecular Dynamics, and Full Relaxation Matrix Refinement," <i>Biochem.</i> , 1994 , <i>33(38)</i> , 11460-11475			
DY				
DZ	Searle, M. S. et al., "On the Stability of Nucleic Acid Structures in Solution: Enthalpy-Entropy Compensations, Internal Rotations and Reversibility," <i>Nucl. Aci Res.</i> , 1993 , <i>21(9)</i> , 2051-2056			
EA	Seela, F. et al., "Palindromic Octa-an Deoxytubercidin: Synthesis, Hairpin Endodeoxyribonuclease <i>Eco</i> RI", <i>Bioc</i>	Formation, and Recog	nition by the	
ЕВ	Shea, R.G. et al., "Synthesis, hybridization properties and antiviral activity of lipid-oligodeoxynucletide conjugates", <i>Nucl. Acids Res.</i> , 1990 , <i>18</i> , 3777-3783 Shiohara et al., "Fixed drug Eruption: Expression of Epidermal Keratinocyte Intercellular Adhesion Molecule-1 (ICAM-1)", <i>Arch. Dermatol.</i> , 1989 , <i>125</i> , 1371-1376			
EC				
ED	Stein, C.A. et al., "Oligodeoxynucleo Review", Cancer Res., 1988, 48, 265		Gene Expression: A	
EE	Stetler-Stevenson, W.G. et al., "Tumo During Invasion and Metastasis," And 1993, 9, 541-573			
EXAMINER		DATE CONSIDER	ED	

6	PE	JC5,	ارج الجار
-	FEB 2	e socs	FOO!
\	PATENITE	TP.NO.P.	*/

Form	PTO-1449 Modified	Docket No. ISIS-4789	Serial No. 09/970,971	
	List of Patent and Publications Cited by Applicant (Use several sheets if necessary)			
	epartment of Commerce t and Trademark Office	Filing Date October 4, 2001	Group Not yet assigned	
ОТНЕ	R DOCUMENTS (Including Author	r, Title, Date, Pertine	nt Pages, Etc.)	
EF	Svinarchuk, F.P. et al., "Inhibition of oligonucleotide conjugated to lipophi	-	-	
EG	Swayze, E. E. et al., "The Synthesis of Mild Reductive Alkylation Procedure Backbone," <i>Synlett</i> , 1997 , 859-861	•		
ЕН	Phosphoramidites: Building Blocks f	E. et al., "The Synthesis of the Sixteen Possible 2'-O-Methyl MMI Dimer midites: Building Blocks for the Synthesis of Novel Antisense otides," <i>Nucleosides & Nucleotides</i> , 1997 , <i>16</i> (7-9), 971-972		
EI	U.S. Congress, Office of Technology Assessment, "The State-of-the-art in Genetic Screening", <i>Genetic Monitoring and Screening in the Workplace</i> , OTA-BA-455, U. Government Printing Office, Washington, D.C., 1990 , Ch. 5, 75-99			
ЕЈ	Uhlmann, E. et al., "Antisense Oligor Chem. Reviews, 1990, 90, 543-584	Uhlmann, E. et al., "Antisense Oligonucleotides: A New Therapeutic Principle", Chem. Reviews, 1990, 90, 543-584		
EK	Wagner, D. et al., "Preparation and S of Nucleosides", J. Org. Chem., 1974	•	ne Organotin Derivatives	
EL	Wagner, R. W. et al., "Antisense Gen Propyne Pyrimidines," Science, 1993		ucleotides Containing C-5	
EM	Wahlestedt, C. et al., "Modulation of Antisense Oligodeoxynucleotides", S	•	<u> </u>	
EN	Wahlestedt, C. et al., "Antisense oligodeoxynucleotides to NMDA-R1 receptor channel protect cortical neurons from excitotoxicity and reduce focal ischaemic infarctions", <i>Nature</i> , 1993 , <i>363</i> , 260-263			
EO	Wilds, C.J. et al., "Duplex Recognition fluoro-D-arabinose and 2'-Deoxy-2'-fluoracts versus Sugar Puckering in the Bioconjugate Chem., 1999, 10, 299-3	luoro-p-ribose. Interm he Stabilization of Trip	olecular 2'-OH-Phosphate	
EXAMINER		DATE CONSIDER	ED	

HB 28 THE		
PATENT O TRACE		Sheet 12 of 21
Form PTO-1449 Modified	Docket No. ISIS-4789	Serial No. 09/970,971
List of Patent and Publications Cited by Applicant (Use several sheets if necessary)	Applicant Manoharan et a	al.

Filing Date

October 4, 2001

DATE CONSIDERED

Group

Not yet assigned

U.S. Department of Commerce

Patent and Trademark Office

EXAMINER

	OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)					
	EP	Wolfe, S., "The Gauche Effect. Some Stereochemical Consequences of Adjacent Electron Pairs and Polar Bonds," <i>Accounts of Chemical Research</i> , 1972, 5, 102-110				
	EQ	Young, S. L. et al., "Triple Helix Formation Inhibits Transcription Elongation In Vitro," <i>Proc. Natl. Acad. Sci. USA</i> , 1991 , 88, 10023-10026				
	ER	Zhang, H. et al., "Conformational Perturbation of the Anticancer Nucleoside Arabinosylcytosine on Z-DNA: Molecular Structure of (araC-dG) ₃ at 1.3 Å Resolution," <i>Biopolymers</i> , 1992 , <i>32</i> , 1559-1569				
*	ES	Ausubel, F.M. et al., in Current Protocols in Molecular Biology, John Wiley, New York, 1989				
*	ET	Cohen in Oligonucleotides: Antisense Inhibitors of Gene Expression, CRC Press, Inc., Boca Raton, FL, 1989				
*	EU	Sambrook, J. et al., <i>Molecular Cloning: A Laboratory Manual</i> , Cold Spring Harbor Labortory Press, 1989				
*	EV	Sanger et al., <i>Principles of Nucleic Acid Structure</i> , Springer-Verlag, New York, NY, 1984				

^{*}A copy of this reference will not be forwarded to the U.S. Patent and Trademark Office since it is believed to be too voluminous and easily obtainable by the Examiner.



Form	PTO-1449 Modified	Docket No. ISIS-4789	Serial No. 09/970,971	
	f Patent and Publications Cited by Applicant everal sheets if necessary)	Applicant Manoharan et al.		
	Department of Commerce at and Trademark Office	Filing Date October 4, 2001	Group Not yet assigned	
ОТНЕ	R DOCUMENTS (Including Author	r, Title, Date, Pertine	nt Pages, Etc.)	
EW	Arnott et al., "Optimised Parameters Biophysical Research Communicatio 1504-1510	•		
EX	Beaucage, S. et al., "Deoxynucleosid Intermediates for Deoxypolynucleotic	-	· · · · · · · · · · · · · · · · · · ·	
EY	Butke, G. et al., "Facile Synthesis of 2'-Amino-2'-Deoxynucleoside from the Corresponding Arabino Derivative," <i>Nucleic Acid Chemistry</i> , Townsend, L.B. et eds., 1986, John Wiley & Sons, New York, 149-152			
EZ	Calvo-Mateo, A. et al., "3'-C-Cyano-3	"Deoxythymidine," Tetra. Letts., 1988, 23, 941-944		
FA	Chen, Q. Y. et al., "Studies on Fluoroalkylation and Fluoroalkoxylation. Part 3: Direct Trifluoromethylation of Aryl Halides with Fluorosulphonyldiflyoromethylodide in the Presence of Copper: an Electron Transfer Induced Process," J. Che Soc. Perkin Trans. I, 1989, 2385-2387 Chladek, S. et al., "Facile Synthesis of 2'-Amino-2'-Deoxyadenosine", J. Carbo. Nucleosides & Nucleotides, 1980, 7, 63-75			
FB				
FC	Codington, J. F. et al., "Nucleosides. Fluorodeoxyuridine, and Other 2'-Ha 1964, 29, 558-564	-	-	
FD	Damha, M. J. et al., "Solution and solid phase chemical synthesis of arabinonucleotides," Can. J. Chem., 1989, 67, 831-839			
FE	Divakar et al., "Reaction Between 2,2 Thiolate Ions", J. Chem. Soc. Perkins			
FF	Divakar et al., "Approaches to the Sy Ribosides", J. Chem. Soc. Perkins Tr		logues of Pyrimidine	
FG	Freskos, J.N., "Synthesis of 2'Deoxyl Catalysis", Nucleosides & Nucleotide			
EXAMINER		DATE CONSIDER	ED	

	FEB 2 6 2002 24		
	Street Parket		Sheet 14 of 21
Form	PTO-1449 Modified	Docket No. ISIS-4789	Serial No. 09/970,971
	f Patent and Publications Cited by Applicant everal sheets if necessary)	Applicant Manoharan et al.	
	Department of Commerce t and Trademark Office	Filing Date October 4, 2001	Group Not yet assigned
ОТНЕ	R DOCUMENTS (Including Author	r, Title, Date, Pertine	nt Pages, Etc.)
FH	Gait, M.J. et al., Oligonucleotide Synt Washington, DC, 1984, Table of Con		roach, IRL Press,
FI	Guschlbauer, W. et al., "Nucleoside of Electronegativity of the Sugar Substitution of the Substitution of the Sugar Substitution of the Sugar Substitution of the Subs		•
FJ	Hansske, F. et al., "2' and 3'-Ketonuc Products," <i>Tetrahedron</i> , 1984 , 40, 12		pino and Xylo Reduction
FK	Hertel, L.W. et al., "Synthesis of 2-D difluoro-D-ribofuranosyl Nucleosides	•	
FL	Hobbs, J. et al., "Polynucleotides Cor 1972, 11, 4336	ntaining 2'-Chloro-2'-D	Deoxyribose", Biochem.,
FM	Ikehara, M., "Purine 8-Cyclonucleosi	des", Accounts Chem.	Res., 1969, 2, 47-53
FN	Ikehara et al., "Purine Cyclonucleosic Purine O-Cyclo-Nucleosides. The Fir Arabinofuranosylguanine", <i>Tetrahedi</i>	st Synthesis of 8,2'-Ar	hydro-8-Oxy 9-β-D-
FO	Ikehara et al., "Polynucleotides. L. sy deoxyadenylic acid) and poly (2'-broi 1977, 4, 4249-4260		- '
FP	Ikehara et al., "Studies of Nucleoside (39). ²⁾ synthesis and properties of 2'ha <i>Bull.</i> , 1978 , <i>26</i> , 2449-2453		-
FQ	Ikehara, M. et al., "Studies of Nucleo 1978 , <i>34</i> , 1133-1138	sides and Nucleotides-	LXXIV ¹ ", Tetrahedron,
FR	Ikehara et al., "Polynucleotides. Ll fluoroadenylic acid)", Nucl. Acids Re		
FS	Hobbs, J., et al., "Polynucleotides con 2'-deoxyribose," <i>Biochemistry</i> , 1973,	_	eoxyribose and 2'-Azido-
EXAMINER		DATE CONSIDER	ED

6	FEI 26 7002 PER TOUR TOUR TOUR TOUR TOUR TOUR TOUR TOU		Sheet 15 of 21
Form	PTO-1449 Modified	Docket No. ISIS-4789	Serial No. 09/970,971
	f Patent and Publications Cited by Applicant everal sheets if necessary)	Applicant Manoharan et al.	
	Department of Commerce at and Trademark Office	Filing Date October 4, 2001	Group Not yet assigned
ОТНЕ	CR DOCUMENTS (Including Author	r, Title, Date, Pertine	nt Pages, Etc.)
FT	Ikehara et al., "Polynucleotides. LV fluoroinosinic Acid", Nucl. Acids Res	-	perties of Poly(2'-deoxy-2'-
FU	Ikehara et al., "Studies on Nucleoside Cyclonucleosides. (43) Synthesis and Chem. Pharm. Bull., 1981, 29(11), 32	Properties of 2'-Halog	
FV	Hobbs, J., et al., "Poly 2'-Deoxy-2'Ar Communications, 1972, 46(4), 1509-		chemical and Biophysical
FW	Imazawa et al., "Nucleosides and Nucl 2'-mercaptouridine and its Derivative		
FX	Inoue, H. et al., "Synthesis and hybrid O-methyl) ribonucleotides", <i>Nucl. Ac</i>		•
FY	Iyer, R. P. et al., "3H-1,2-Benzodithic Sulfurizing Reagent in the Solid-Phase Phosphorothioates," J. Am. Chem. So	se Synthesis of Oligod	eoxyribonucleoside
FZ	Jarvi, E. T. et al., "Synthesis and Containing a Difluoromethylene Unit		
GA	Jones, R.A., "Transient protection: Endeoxynucleosides", J. Am. Chem. So		
GB	Kazimierczuk et al., "Synthesis of 2'-2'-deoxynucleosides via novel direct procedure", J. Am. Chem. Soc., 1984,	stereospecific sodium	•
GC	Koole et al., "Synthesis of phosphate-fluorenylmethoxycarbonyl as transier 54, 1657-1664		
GD	Markiewicz, W. and Wiewiorowski, Townsend, L. and Tipson, eds., J. Wi		· · ·
EXAMINER		DATE CONSIDER	ED

	A SERVICE OF THE SERV		Sheet 16 of 21
Form	PTO-1449 Modified	Docket No. ISIS-4789	Serial No. 09/970,971
	of Patent and Publications Cited by Applicant everal sheets if necessary)	Applicant Muthiah Manohara	n et al.
1	Department of Commerce nt and Trademark Office	Filing Date October 4, 2001	Group Not yet assigned
ОТН	ER DOCUMENTS (Including Author	r, Title, Date, Pertine	nt Pages, Etc.)
GE	Markus-Sekura et al., "Comparative of Gene Expression by Antisense Oligo Phosphotriester, Methylphosphonate <i>Res.</i> , 1987 , <i>15(4)</i> , 5749-5763	nucleotide Analogues	Having Alkyl
GF	Miller, P.S. et al., "A New Approach to Chemotherapy Based on Molecular Biology and Nucleic Acid Chemistry: Matagen (Masking Tape for Gene Expression", <i>Anti-Cancer Drug Design</i> , 1987 , <i>2</i> , 117-128		
GG	Ohtsuka, M. et al., "Recognition by Restriction Endonuclease <i>Eco</i> RI of Deoxyoctanucleotides Containing Modified Sugar Moieties", <i>Eur. J. Biochem.</i> , 198-139, 447-450		
GH	Parkes, K.E.B. et al., "A Short Synthesis of 3'-Cyano-3'-Deoxythymidine", Tetra. Lett., 1988, 29, 2995-2996		
GI	Raganthan, R., "Modification of the 2 21-a-Substituted-21-Deoxyadenosine		-
GJ	Rao, T. S. et al., "A Novel One-step 2,3'-Anhydrothymidine," <i>J. Chem. Sci.</i>		
GK	Robins, M. J. et al., "Nucleic acid related compounds. 41. Restricted furanose conformations of 3',5'-O-(1,1,3,3,-tetraisopropyldisilox-1,3-diyl) nucleosides provide a convenient evaluation of anomeric configuration," Can. J. Chem., 1983, 61, 1911-1920		
GL	Ryan et al., "Synthesis of 2-Thio-D-ribose and 2'-Thioadenosine Derivatives", J. Org Chem., 1971, 36(18), 2646-2657		
GM	Shibahara et al., "Inhibition of human synthetic oligo-RNA derivatives", Na		
GN	Sproat, B.S. et al., "Highly Efficient methyloligoribonucleotides and Tetra Resistant to Degradation by RNA or 1989, 17, 3373-3386	abiotinylated Derivativ	es; Novel Probes that are

EXAMINER

DATE CONSIDERED

			511001 17 01 21	
Form	PTO-1449 Medified	Docket No. ISIS-4789	Serial No. 09/970,971	
	f Patent and Publications Cited by Applicant everal sheets if necessary)	Applicant Manoharan et al.		
	Department of Commerce t and Trademark Office	Filing Date October 4, 2001	Group Not yet assigned	
ОТНЕ	R DOCUMENTS (Including Author	r, Title, Date, Pertine	nt Pages, Etc.)	
GO	Sproat, B. S. et al., "New synthetic 3'-O-phosphoramidites using a nov 18, 41-49	• •	•	
GP	Uesugi, S. et al., "A Linear Relationship Between Electronegativity of 2'-Substituents and Conformation of Adenine Nucleosides," <i>Tetrahedron Letts</i> . 42, 4073-4076			
GQ	1	s of 2'-Fluoro-2'-Deoxyadenosine and Synthesis and 3',5'-Cyclic Phosphate Derivative", <i>Nucleosides &</i>		
GR	Uhlmann et al., "Antisense Oligon Rev., 1990, 558	nucleotides: A New Therapeutic Principle", Chem.		
GS	Zon, G., "Oligonucleotide analogu Pharmaceutical Res., 1988, 5(9), 5		nerapeutic agents,"	
GT		Influence of RNA Incorporation in DNA: esonance Refinement of d (CG)r(CG)d(CG) and		
GU				
GV	Nishizaki, T. et al., "Solution Structured Hybrid Region, d(GG)r(AGAU)d(d(GGAGA)r(UGAC)•d(GTCATC)	GAC)•d(GTCATCTC(C) and	
EXAMINER		DATE CONSIDER	ED	
		•		

		- Land	<u> </u>		<u> </u>	Sheet 18 of 21
Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary)			Docket No. ISIS-4789	Serial No 09/970,9		
			Applicant Manoharan et al.	1 **		
	U.S. Department of Commerce Patent and Trademark Office			Filing Date October 4, 2001	Group Not yet a	ssigned
		U. S	S. PATENT D	OCUMENTS		
Examiner Initial		Document No.	Date	Name	Class	Subclass
	GW	3,687,808	08/29/72	Merigan et al.	195	28
	GX	4,689,320	08/25/87	Kaji	514	44
	GY	4,806,463	02/21/89	Goodchild et al.	435	5
	GZ	5,004,810	04/02/91	Draper	536	27
	HA	5,166,195	11/24/92	Ecker	514	44
	нв	5,194,428	03/16/93	Agrawal et al.	514	44
	нс	5,212,295	05/18/93	Cook	536	26.7
	HD	5,242,906	09/07/93	Pagano et al.	514	44
	HE	5,248,670	09/28/93	Draper et al.	514	44
	HF	5,442,049	08/15/95	Anderson et al.	536	24.5
(4)	HG	5,457,189	10/10/95	Crooke et al.	536	24.5
	нн	5,514,577	05/07/96	Draper et al.	435	238
	ні	5,514,788	05/07/96	Bennett et al.	536	23.1
	НЈ	5,523,389	06/04/96	Ecker et al.	536	23.1
		FORE	IGN PATENT	DOCUMENTS		
Examiner Initial	I I		Country	YES Tr	anslation NO	
	нк	WO 89/12060	12/14/89	PCT		
	HL.	WO 94/08003	04/14/94	.PCT		
	НМ	WO 92/03568	03/05/92	PCT		
EXAMINE	R			DATE CONSIDE	RED	

		PATE	MARY			Sheet 19 of 21	
Form PTO-1449 Modified			Docket No. ISIS-4789	Serial No 09/970,9			
List of Patent and Publications Cited by Applicant (Use several sheets if necessary)				Applicant Manoharan et al.			
		epartment of Comm and Trademark Off		Filing Date October 4, 2001	Group Not yet a	assigned	
		U.	S. PATENT D	OCUMENTS	•		
Examiner Initial		Document No.	Date	Name	Class	Subclass	
	HN	5,580,767	12/03/96	Cowsert et al.	435	172.3	
	но	5,582,972	12/10/96	Lima et al.	435	6	
	HP	4,381,344	04/1983	Rideout et al.	435	87	
	HQ	5,013,830	05/07/91	Ohtsuka et al.	536	27	
	HR	5,134,066	07/28/92	Rogers et al.	435	91	
	HS	5,212,295	05/18/93	Cook	536	26.7	
	ĤТ	5,214,135	05/25/93	Srivastava et al.	536	26.7	
	HU	5,466,786	11/14/95	Buhr et al.	536	26.26	
	HV	5,658,731	08/19/97	Sproat et al.	435	6	
	HW	5,672,695	09/30/97	Eckstein et al.	536	24.5	
	HX	5,698,687	12/16/97	Eckstein et al.	536	25.3	
		FORI	EIGN PATENT	T DOCUMENTS	_	· _ _	
Examiner Initial		Document No.	Date	Country	YES Tr	anslation NO	
	HY	2,017,369	05/23/90	Canada	X		
	HZ	0 260 032	08/27/87	EP	X		
	IA	0 287 313	10/19/88	EP	X		
	IB	0 399 330	05/15/90	EP		X	
	IC	0 417 999	03/10/91	EP	X		
EXAMINE	R			DATE CONSIDE	RED		

			NEW .			Sheet 20 of 21	
Form PTO-1449 Wodified				Docket No. ISIS-4789	Serial No. 09/970,971		
List of Patent and Publications Cited by Applicant (Use several sheets if necessary)				Applicant Manoharan et al.			
U.S. Department of Commerce Patent and Trademark Office			Filing Date October 4, 2001	Group Not yet assigned			
		U.	S. PATENT D	OCUMENTS			
Examiner Initial		Document No.	Date	Name	Class	Subclass	
	ID	5,245,022	09/14/93	Weis et al.	536	24	
	IE	5,627,053	05/06/97	Usman et al.	435	91	
	IF	5,639,647	06/17/97	Usman et al.	435	199	
	IG	5,817,635	10/06/98	Eckstein et al.	514	44	
1-11-11-11-11-11-11-11-11-11-11-11-11-1	IH	5,859,221	01/12/99	Cook et al.	536	23	
		FORE	IGN PATENT	DOCUMENTS	•	•	
Examiner Initial		Document No.	Date	Country	Translation YES NO		
	II	39 15462 A1	06/09/90	Germany		X	
	IJ	41 10085 A1	10/01/92	Germany		X	
	IK	WO 90/15814	12/27/90	PCT	X		
	IL	WO 91/06556	05/16/91	PCT	X		
	IM	WO 91/15499	10/17/91	PCT		X	
	IN	WO 92/07065	04/30/92	PCT	X		
	Ю	339 842	11/02/89	EP			
	IP	0 552 178 B1	01/02/97	EP			
	IQ	1 205 021	05/27/86	Canada			
EXAMINER				DATE CONSIDE	DATE CONSIDERED		



Form	PT(D-144	9 Ma	dified
------	-----	--------------	------	--------

List of Patent and Publications Cited by Applicant (Use several sheets if necessary)

U.S. Department of Commerce Patent and Trademark Office

Docket No.	
ISIS-4789	

Serial No. **09/970,971**

Applicant

Manoharan et al.

Filing Date Group

October 4, 2001 Not yet assigned

U. S. PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Name	Class	Subclass
	IR	5,582,986	12/10/96	Monia et al.	435	6
	IS	5,591,600	01/07/97	Ecker	435	69.1
	IT	5,591,623	01/07/97	Bennett et al.	435	240.2
	IU	5,591,720	01/07/97	Anderson et al.	514	44
	IV	5,607,923	03/04/97	Cook et al.	514	44
	IW	5,620,963	04/15/97	Cook et al.	514	44
	IX	5,639,649	06/17/97	Almond et al.	435	235.1
	IY	5,658,891	08/19/97	Draper et al.	514	44
	IZ	5,661,134	08/26/97	Cook et al.	514	44
	JA	5,681,747	10/28/97	Boggs et al.	435	375
	JB	5,681,944	10/28/97	Crooke et al.	536	24.5
	JC	5,877,309	03/02/99	McKay et al.	536	24.5
	JD	5,985,558	11/16/99	Dean et al.	435	6
	JЕ	5,955,443	09/21/99	Bennett et al.	514	44
	JF	6,111,094	08/29/00	Bennett et al.	536	24.5
	JG	5,334,711	08/02/94	Sproat, et al.	536	24.5
	JH	6,300,491	10/09/01	Bennett et al.	536	24.5
	Л	5,670,633	09/23/97	Cook et al.	536	23.1
	JJ	6,307,040	10/23/01	Cook et al.	536	24.5
EXAMINER			DATE CONSIDE	DATE CONSIDERED		